Advisory Committee to the Director

An Accelerated Pathway Towards a Universal Influenza Vaccine

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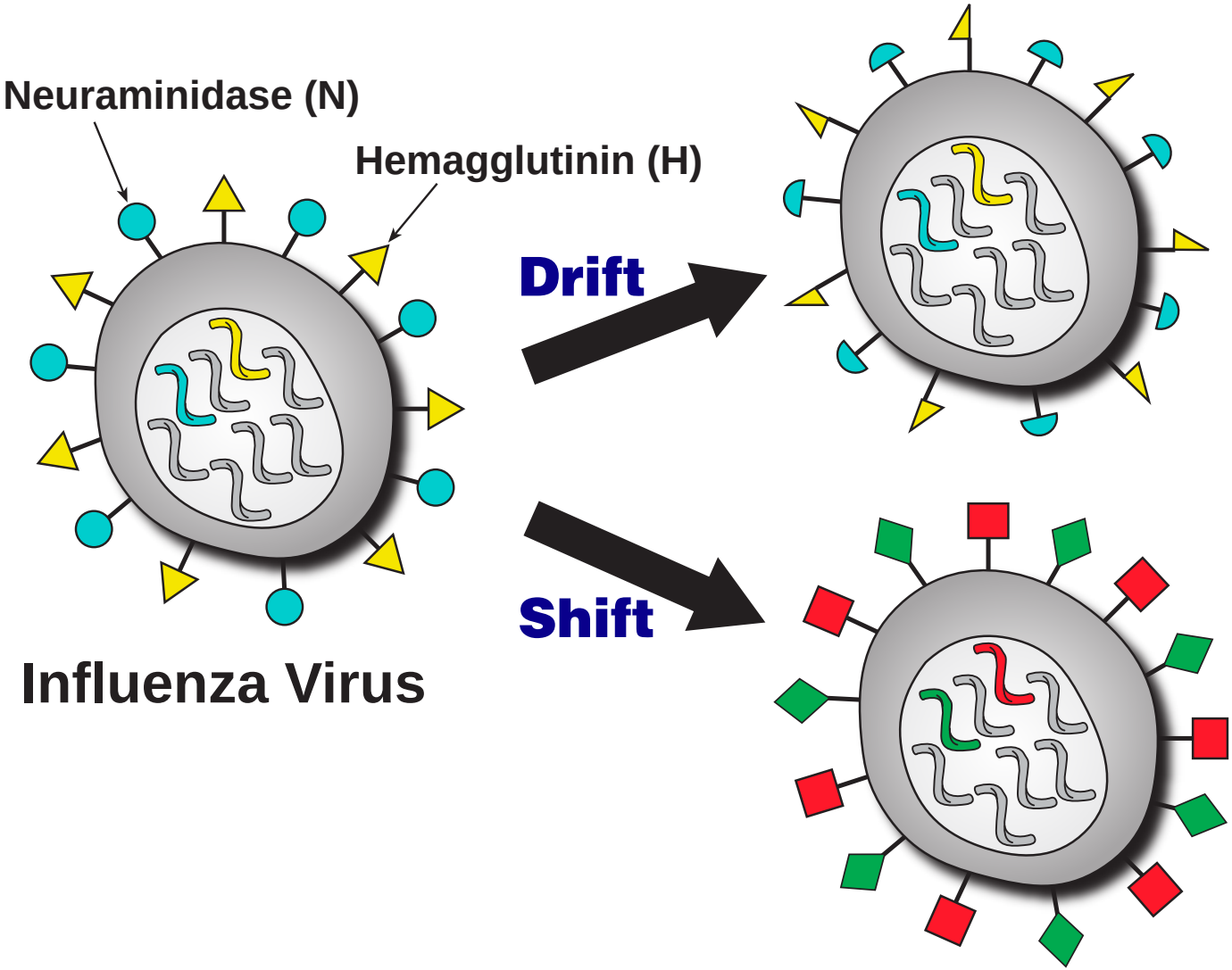
June 8, 2017

National Institute of Allergy and Infectious Diseases

Seasonal vs. Pandemic Influenza



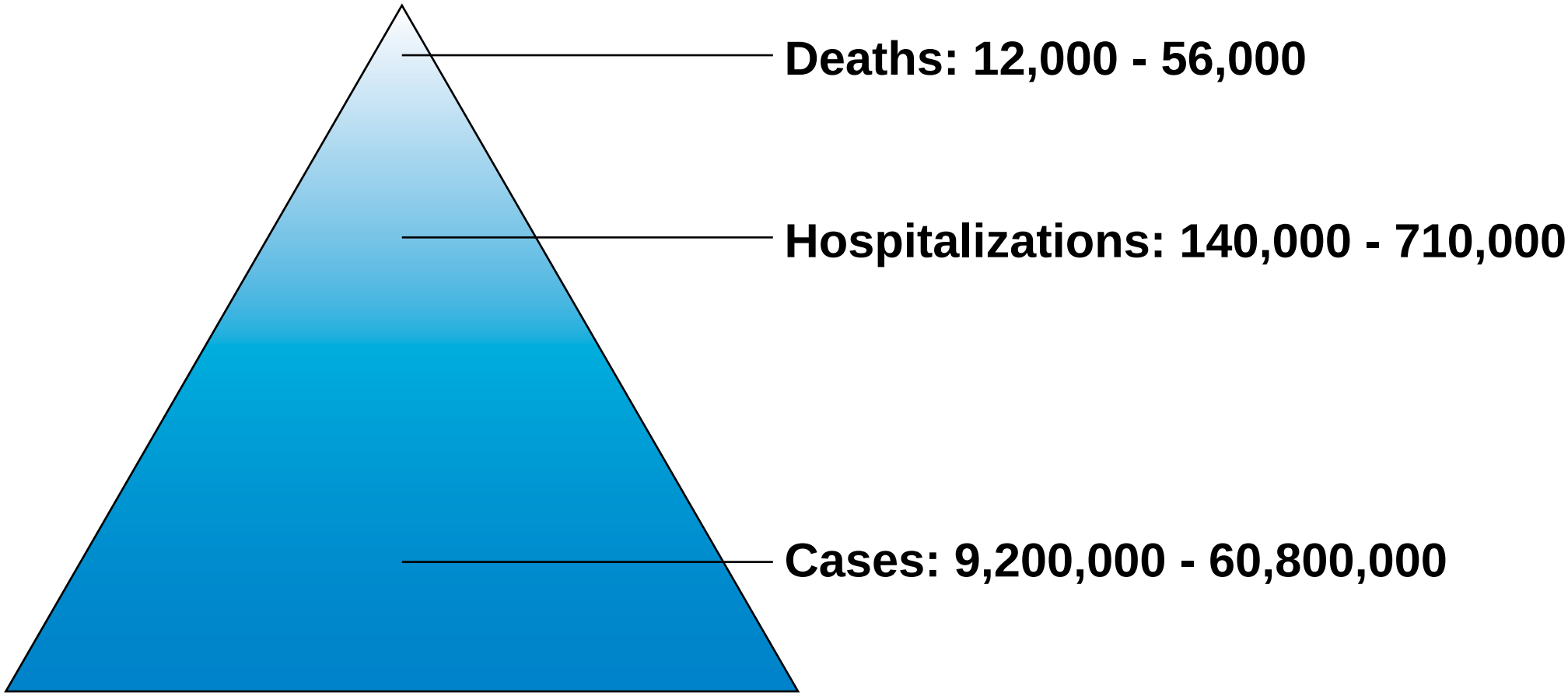
Seasonal Influenza

- Annual occurrence
- Residual immunity in population

Pandemic Influenza

- Unpredictable rare occurrence
- “Naïve” population

Annual Disease Burden of Seasonal Influenza in the United States



Source: CDC. Annual estimates since 2010

Influenza Pandemics in the 20th–21st Centuries

1918	H1N1	“Spanish Flu”	~50 million deaths
1957	H2N2	“Asian Flu”	1-2 million deaths
1968	H3N2	“Hong Kong Flu”	700,000 deaths
2009	H1N1	“Swine Flu”	284,500 deaths

- **Current seasonal influenza vaccines are not consistently effective**
- **Pandemics do occur and response after the fact is not effective**
- **“Chasing after” potential pandemic outbreaks (pre-pandemic viruses) is costly and ineffective**

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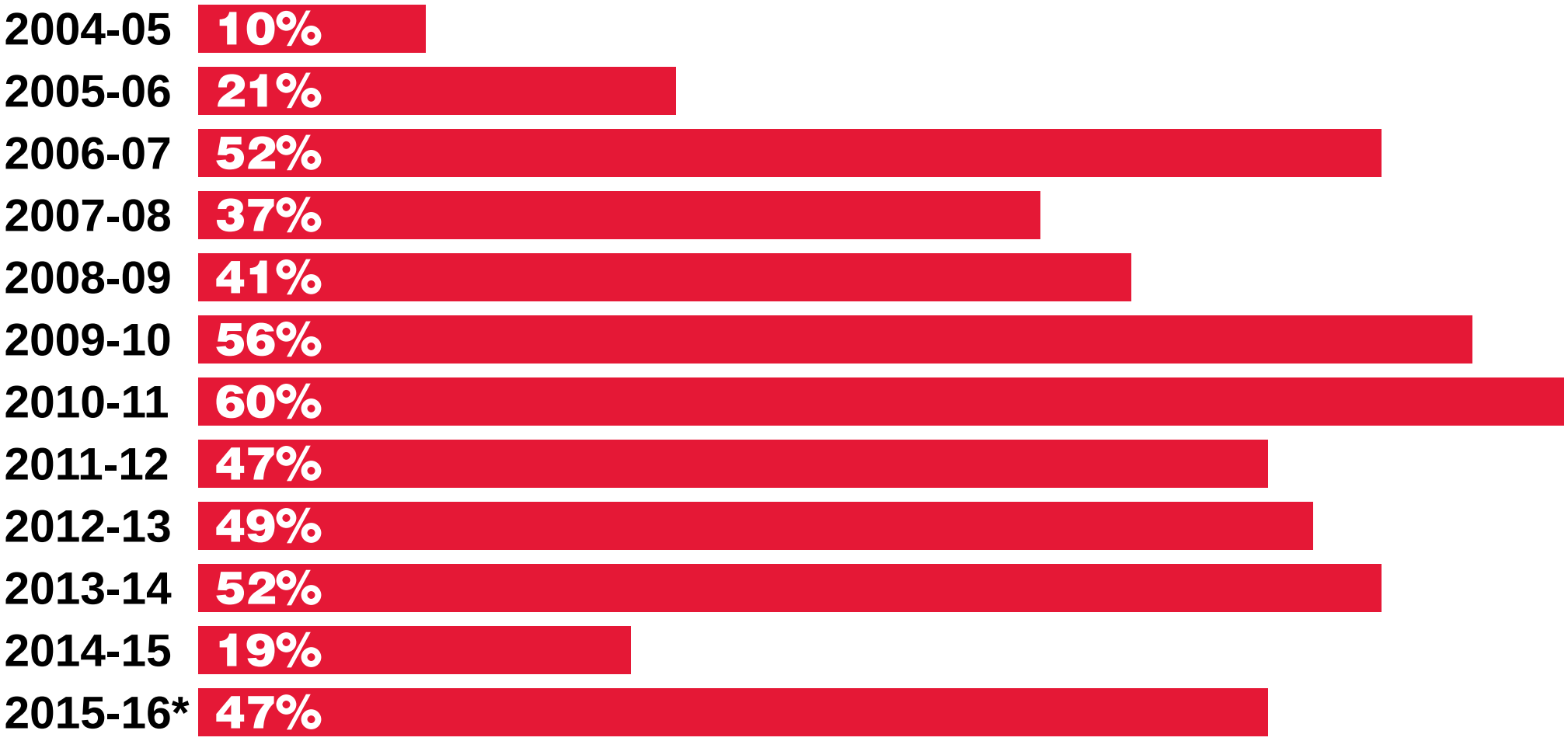
Adjusted Vaccine Effectiveness Estimates for Influenza Seasons from 2005-2016



*Estimate from Nov 2, 2015–April 15, 2016.

Source: CDC.gov

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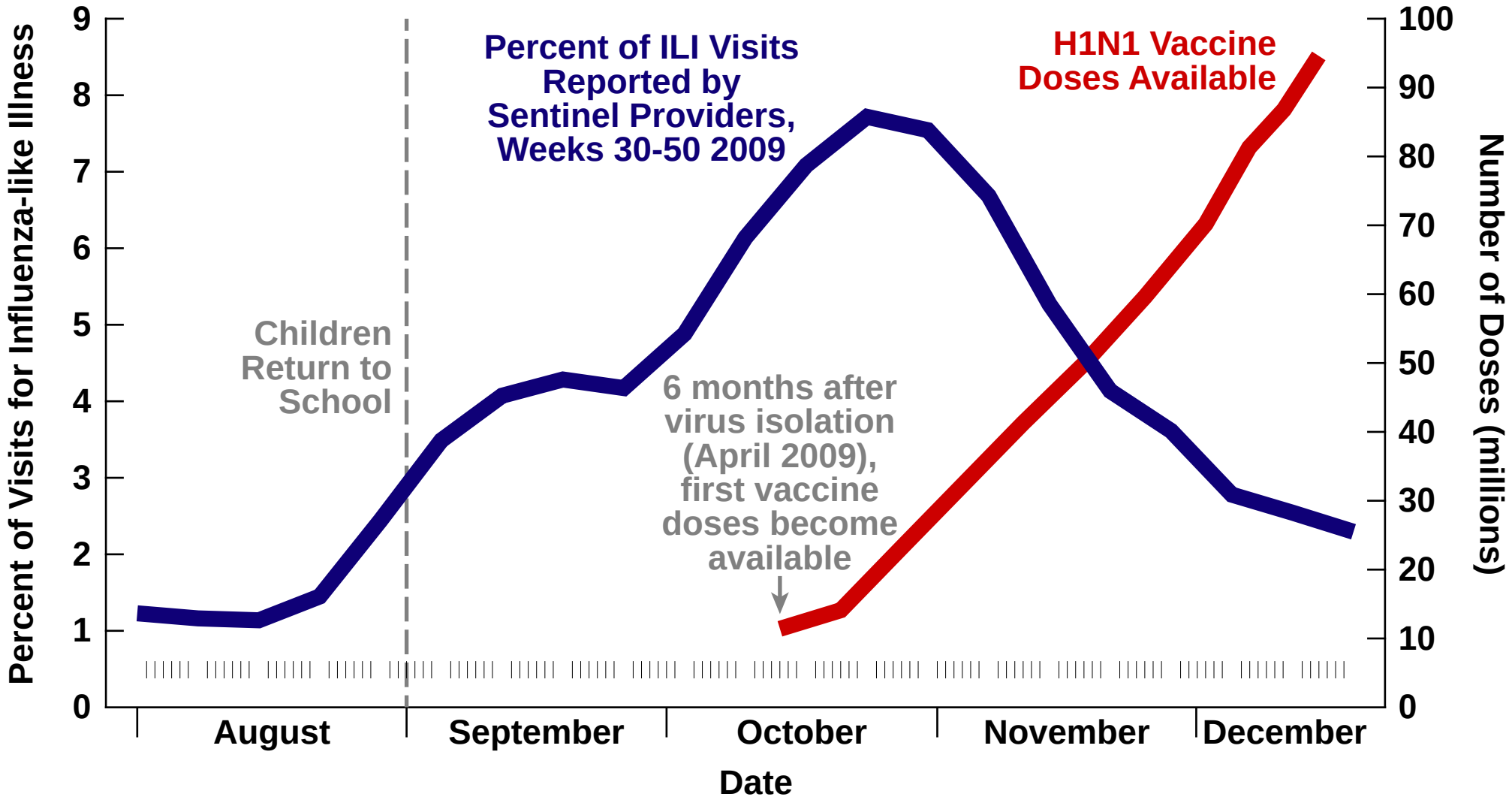
Vaccine Lags Behind 2009 H1N1 Influenza Pandemic



- **Current seasonal influenza vaccines are not consistently effective**

- **Pandemics do occur and response after the fact is not effective**

- **“Chasing after” potential pandemic outbreaks (pre-pandemic viruses) is costly and ineffective**

- **Pre-Pandemic vaccines:** against circulating strains that *threaten* to cause a pandemic (e.g., H5N1, H7N9)

- **Pandemic vaccines:** against strain causing an *existing* pandemic (e.g., 2009 H1N1)

The New England Journal of Medicine

Established in 1812 as THE NEW ENGLAND JOURNAL OF MEDICINE AND SURGERY

VOLUME 353 SEPTEMBER 29, 2005 NUMBER 13

REVIEW ARTICLE

Avian Influenza A (H5N1) Infection in Humans

The Writing Committee of the World Health Organization (WHO) Consultation on Human Influenza A/H5

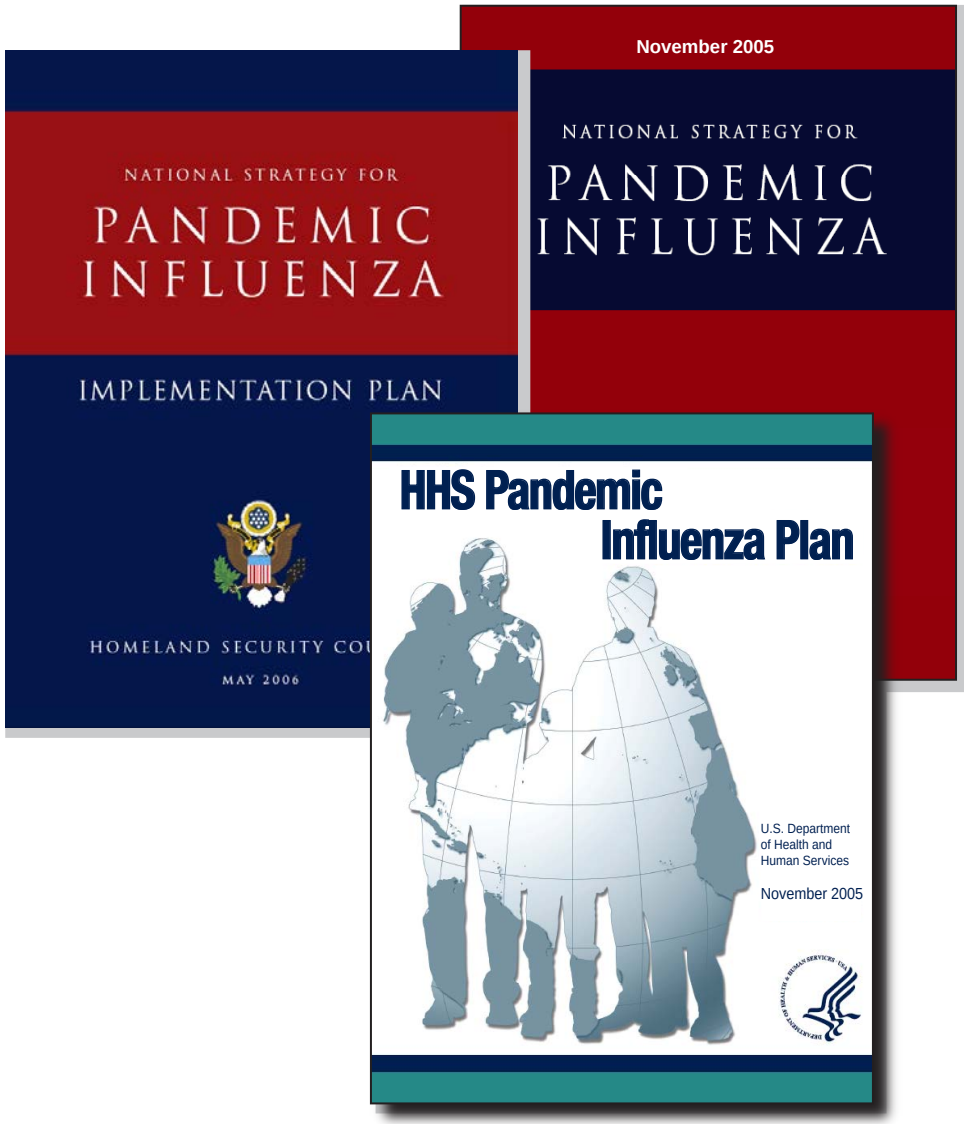
The New York Times

November 1, 2005

Bush Calls for $7.1 Billion to Prepare for Bird Flu Threat

President Bush today unveiled a strategy to combat the threat of an avian flu pandemic, calling for $7.1 billion in emergency spending to stockpile reserves of medicines and to press ahead with the development of a new vaccine.

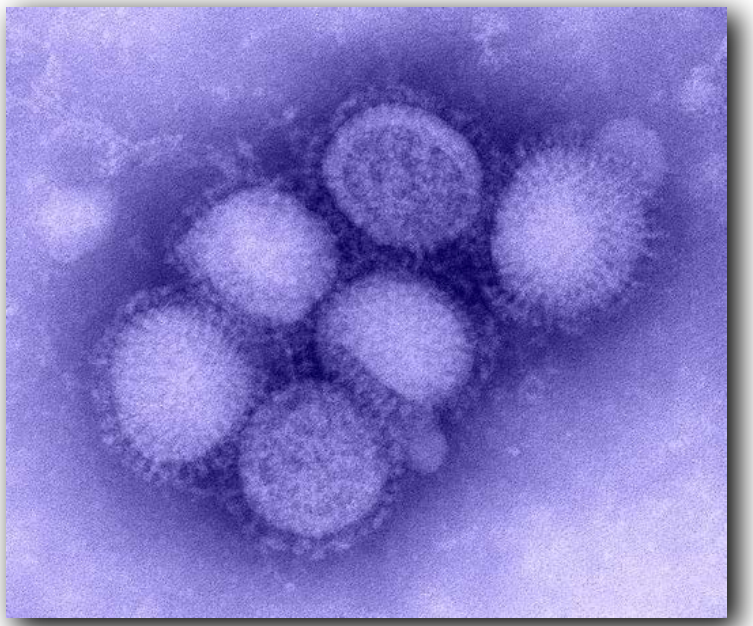
Pandemic Influenza Preparedness
Strategy and Implementation

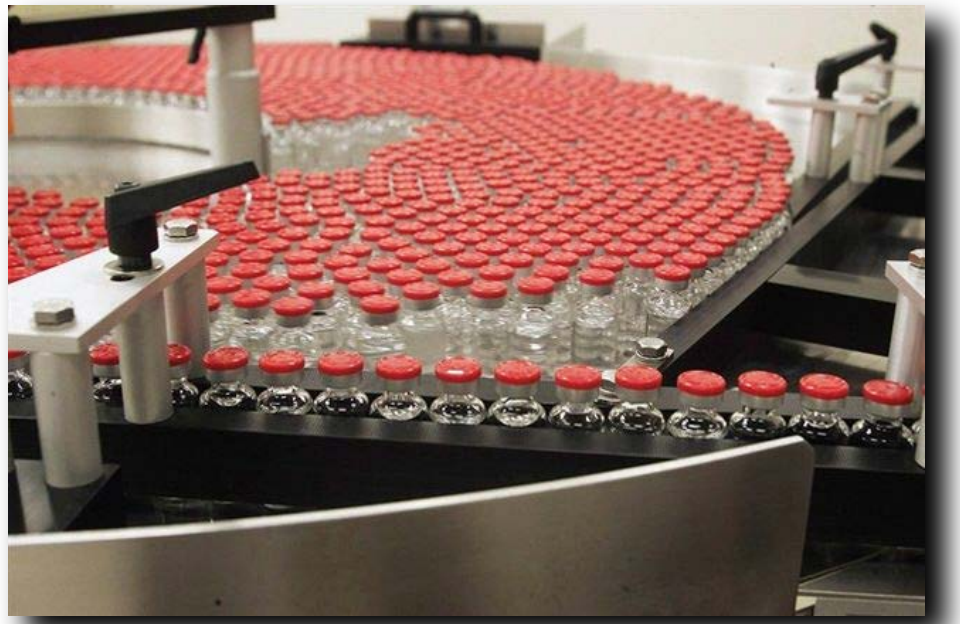


- International Surveillance
- Domestic Surveillance
- Vaccines
- Antivirals
- Communications
- State and Local Preparedness

FDA Approves First Adjuvanted H5N1 Influenza Vaccine for U.S. Stockpile

- Approved Nov. 22, 2013
- Made by ID Biomedical (GSK subsidiary)
- Includes AS03 adjuvant





Phase 2 Trials of 2013 H7N9 Vaccine in Healthy Adults

Serological Responses to an Avian Influenza A/H7N9 Vaccine Mixed at the Point-of-Use With MF59 Adjuvant

A Randomized Clinical Trial

MJ Mulligan, DI Bernstein, P Winokur et al

Effect of Varying Doses of a Monovalent H7N9 Influenza Vaccine With and Without AS03 and MF59 Adjuvants on Immune Response

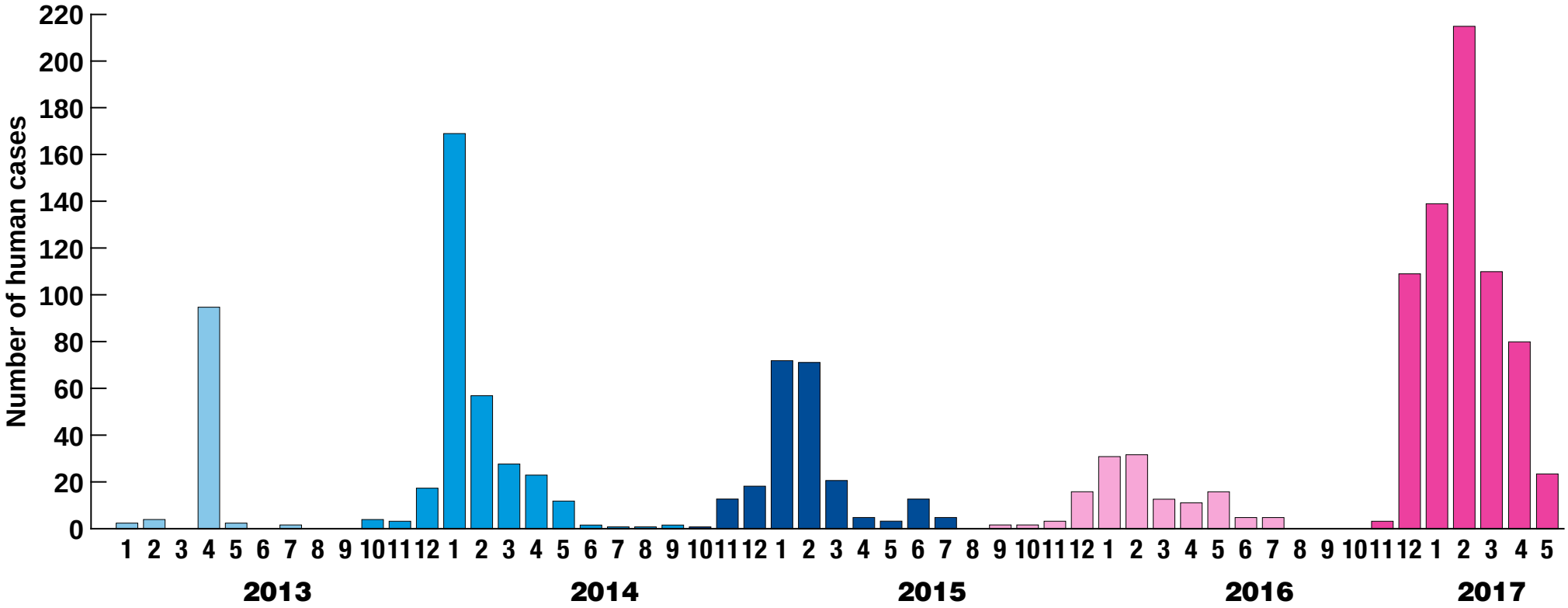
A Randomized Clinical Trial

LA Jackson, AR Bellamy et al

- ***Acceptable safety profile; two adjuvanted doses needed to induce adequate immune response***

Five Waves of Human H7N9 Influenza Infections in China, February 2013-present

- **1,486** confirmed human cases, **559** deaths
- 5th wave: >40% of cumulative cases



Source: FAO, 5/10/2017

Improving seasonal influenza vaccines

Pandemic influenza vaccines

Universal influenza vaccines

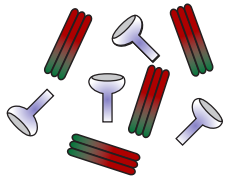
Improving seasonal influenza vaccines

Pandemic influenza vaccines

Universal influenza vaccines

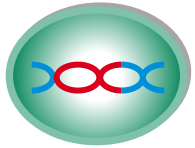
Evolution of Technologies for Influenza Vaccines

New Platforms for Seasonal and Pandemic Influenza Vaccines

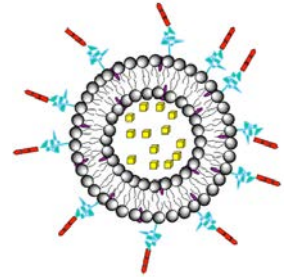


Recombinant subunit

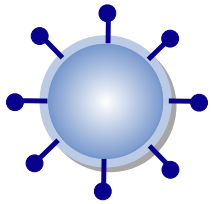
Synthetic peptide



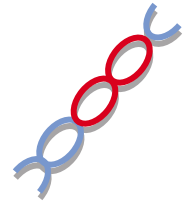
Microbial vector



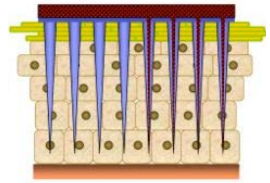
Nanoparticle-based



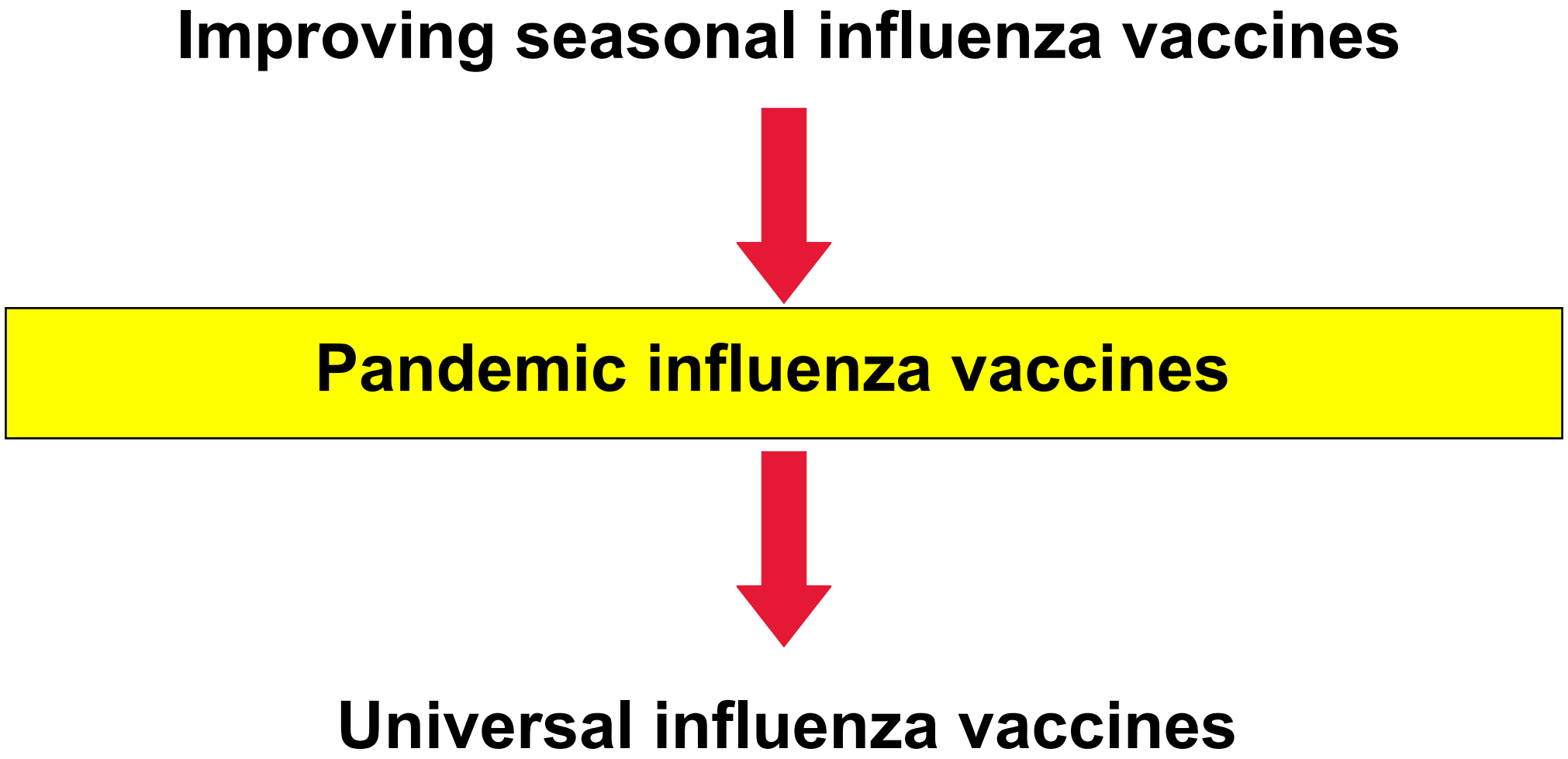
Virus-like particles (VLPs)



DNA-based

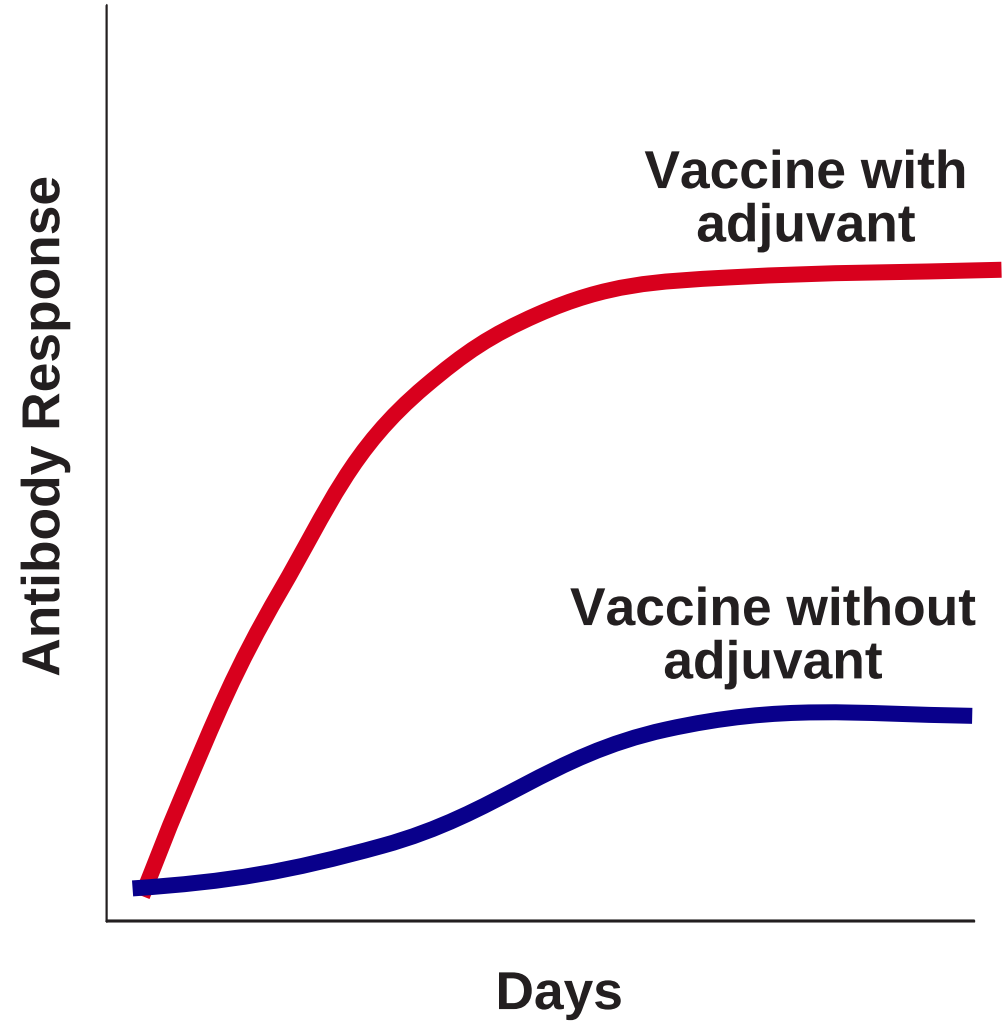


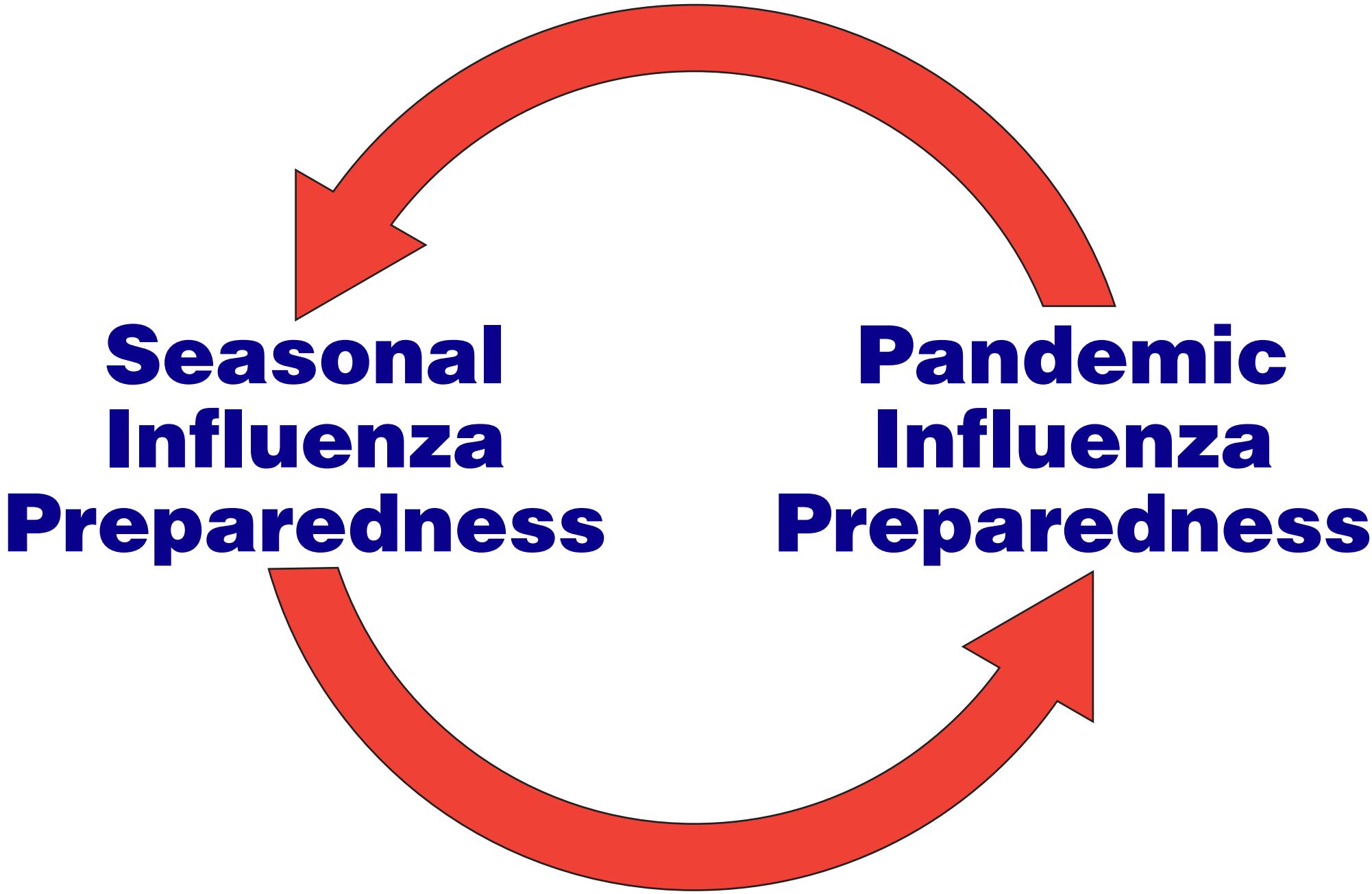
Novel delivery systems (e.g., microneedles)


Improving seasonal influenza vaccines
Pandemic influenza vaccines
Universal influenza vaccines

Vaccine Adjuvants

- Reduce amount of antigen needed
- Promote earlier, stronger, more durable immune responses
- May increase cross-protective immune response




Seasonal Influenza Preparedness
Pandemic Influenza Preparedness

Improving seasonal influenza vaccines

Pandemic influenza vaccines

Universal influenza vaccines

nature medicine
December 2010
Volume 16 No 12

Induction of Unnatural Immunity: Prospects for a Broadly Protective Universal Influenza Vaccine

GJ Nabel and AS Fauci

Goals for Universal Influenza Vaccines

- **Breadth** to cover future drifted and pandemic strains

- **Durability** ≥5 years

National Institute of Allergy and Infectious Diseases | NIAID Conference

Pathway to a Universal Influenza Vaccine

June 28-29, 2017
Rockville, MD

Key Workshop Topics/Gaps in Knowledge

- Goals of a universal vaccine program
- Epidemiology, transmission, natural history, and pathogenesis of influenza
- Protective immune mechanisms in influenza
- Pre-existing immunity to influenza; impact on infection and response to vaccination

Key Workshop Topics/Gaps in Knowledge (cont.)

- Universal vaccine platforms for influenza
- Diagnostics for assessing mechanisms of immune protection in influenza
- Animal models in influenza research
- Human influenza challenge model

Previous Examples of Catalyzing NIH Vaccine Initiatives

- NIAID Vaccine Research Center – Intramural
- NIAID Center for HIV/AIDS Vaccine Immunology (CHAVI)
- NIAID Centers for HIV/AIDS Vaccine Immunology and Immunogen Discovery (CHAVI-ID)

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NIAID Vaccine Research Center

VRC Senior Investigators

Basic Research → **Clinical Trials**

VRC Research: From HIV to Zika

- HIV
- West Nile virus
- Chikungunya
- Ebola/Marburg
- Influenza
- Malaria
- MERS-CoV
- RSV
- Tuberculosis
- Venezuelan, Eastern, and Western equine encephalitis viruses
- Zika

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Center for HIV/AIDS Vaccine Immunology (CHAVI)

- Consortium supported 2005-2012
- Multidisciplinary teams
- Multi-pronged approaches addressing key scientific challenges
- Frequent meetings
- Information sharing
- Collaborative projects

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CHAVI - ID

- **Duke Center for HIV/AIDS Vaccine Immunology and Immunogen Discovery**

- **Scripps Center for HIV/AIDS Vaccine Immunology and Immunogen Discovery**

An NIH-led, bold initiative towards the development of a universal influenza vaccine